REMARKS

Amendments to the Claims

Claims 1 to 74 are pending. The present amendment cancels Claims 27, 29 to 34, 36, 37, 53, 61 and 64 to 67, amends Claims 28 and 35 and adds new Claims 75 to 79.

Applicants reserve the right to file continuation applications with claims directed to the subject matter of cancelled Claims 27, 29 to 34, 36, 37, 53, 61 and 64 to 67.

Support for new Claims 75 to 79 are found in originally-filed Claims 1 to 74 and in the specification as follows:

New Claims 75-79	Original Claims 1-74	Specification (page/line)
75	66	p.29/l.11,24-32
76	66	p.29/l.11,24-32
77	66	p.29/l.11,24-32
78	66	p.29/l.11,24-32
79	66	p.29/l.11,24-32

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I. Amended Claim 28

The sole pending independent claim (Claim 28) now specifies a method for treating or inhibiting restenosis resulting from angioplasty, the method comprising:

(i) placing an endolumenal stent in the artery at the site of the angioplasty;

(ii) wherein the stent comprises eplerenone.

Support for the claim amendment can be found in originally-filed Claims 64 to 66 and in the specification as filed at, for example, page 29, lines 11 and 24-32.

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II. Rejection Under 35 USC §112(1)

The Office has rejected originally-filed Claims 27-37, 53 and 64-67 under 35 USC 112, first paragraph for failing to provide enablement in the specification for "prevention" of restenosis. Applicants have deleted "prevention" from amended, sole-independent Claim 28 submitted herein.

III. Rejection Under 35 USC §112(2)

The Office has rejected originally-filed Claim 29 under 35 USC 112, second paragraph, asserting that use of the term "substantially" renders the claim indefinite. Applicants have cancelled Claim 29 and therefore the rejection is moot.

IV. Rejection Under 35 USC §103(a)

The Office has rejected originally-filed Claims 27-37, 53 and 64-67 under 35 USC 103(a) as being unpatentable over Baim and Grossman ("Baim") in view of Delyani(A) and Delyani(B). Applicants respectfully disagree and request withdrawal of this rejection.

It is well accepted (e.g., MPEP §2142) that in order to establish a prima facie case of obviousness the Office must show:

(1) there is some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings,

(2) there is a reasonable expectation of success if the modification or combination is carried out, and

(3) the reference, or references when combined, teach or suggest all the claim limitations.

Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicants' disclosure. Delyani(A), Delyani(B) and "Baim", either alone or in combination, do not teach or suggest the claimed invention, and do not provide a reasonable expectation of success if the asserted modification were carried out.

Claim 28 (the sole, remaining independent claim rejected under §103) of the present application has been amended to specify that the method involves:

(a) treating or inhibiting restenosis resulting from angioplasty, the method comprising:

(b) placing an endolumenal stent in the artery at the site of the angioplasty;

(c) wherein the stent comprises eplerenone.

Delyani(A) is a published abstract describing a study evaluating the effect of eplerenone in a rat model of cardiac muscle tissue (myocardium) ischemia. The ischemic myocardium in the rat model was produced by tying off the left coronary artery, in order to block blood flow into the muscle and induce ischemic damage to a specific region of cardiac muscle. The Office mistakenly characterizes myocardial infarction (ischemia in cardiac muscle tissue) as a study of vascular injury. The study was actually focused on the effect of eplerenone on (a) cardiac muscle (myocardial) wound healing, and (b) left ventricular (muscle wall) remodeling in their rat model. The end points used in the study were (a) thinning of the infarcted muscle wall (myocardium), (b) collagen volume fraction of the infarcted and

noninfarcted cardiac muscle tissue, and (c) diastolic pressure/volume relationship.

In addition, the results reported in Delyani(A) indicate that eplerenone and vehicle had a similar effect on the collagen volume fraction in the injured (infarcted) region of the cardiac muscle tissue, i.e. eplerenone was no better than no treatment regarding collagen changes in injured tissue. Treatment with eplerenone, however, produced a decrease in cardiac muscle collagen in healthy, non-injured regions of the myocardium, relative to vehicle treatment. This observation was also recognized by the Office (at page 8, lines 1-2 of the Office Action). However, applicants wish to point out that this observation actually teaches <u>away</u> from treating injured tissue (heart muscle or otherwise) with eplerenone to affect a decrease in collagen levels---collagen levels decreased <u>only</u> in the non-injured regions of the heart muscle treated with eplerenone. Based on the results reported in Delyani(A) one would not expect eplerenone to be effective at reducing restenosis at the site of an injury such as an angioplasty.

Further, Delyani(A) does not describe, or even mention angioplasty, restenosis or any pathogenic change in a blood vessel, nor does it describe or even mention use of a stent or a stent comprising eplerenone to treat or inhibit restenosis in an artery. Instead, Delyani(A) teaches that eplerenone is without effect on collagen deposition in injured (infarcted) heart muscle, thus pointing one skilled in the art away from using eplerenone to reduce fibrosis in injured tissue, such as at the site of an angioplasty.

Delyani(B) is a review article describing treatment of heart failure, a condition in which the heart muscle fails to function properly. Like Delyani(A), the studies involving fibrosis in Delyani(B) concern collagen in the heart muscle, not the vasculature. Delyani(B) does not describe, or even mention angioplasty, restenosis or any pathogenic change in a blood vessel, nor does it describe or even mention use of a stent or a

stent comprising eplerenone to treat or inhibit restenosis in an artery. Instead, Delyani(A) teaches that aldosterone antagonism can improve heart function through direct effects on heart muscle, not the vasculature. Further, as noted at page 755, column 1 second paragraph of Delyani(B) (noted also in the Office Action), it is pointed out that studies on the effect of aldosterone antagonism in blocking collagen synthesis are contradictory (reference 27 versus reference 28), concluding that "[c]learly more work is needed in order to clarify this issue. . .". Such reporting of contradictory results, along with the ineffectiveness of eplerenone on collagen synthesis at an injury site as reported in Delyani (A), would not lead one to using a stent comprising eplerenone to treat restenosis at a site of injury following arterial angioplasty.

In addition, it should be noted that in both Delyani(A) and Delyani(B) eplerenone is dosed orally and produces systemic effects throughout the body. In contrast, applicants' novel aspect of administering eplerenone locally in a stent reduces any adverse effects that might be associated with systemic eplerenone administration.

"Baim" describes use of angioplasty to treat stenoses in coronary arteries. "Baim" also describes the use of intravascular stents in angioplasty. However "Baim" points out that "stenting does not reduce the amount of local intimal hyperplasia" (see page 987, column 2, first paragraph) and that "[t]o date, despite substantial effort, no mechanical or pharmacologic strategy has substantially reduced this restenosis rate" (see page 986, column 2, last paragraph). Thus "Baim" points out the urgent, unfulfilled medical need for applicants' invention and the fact that no such pharmacologic or mechanical treatment exists.

Thus, without the improper use of hindsight, based on applicants' specification and drawings, the teachings in Delyani (A), Delyani(B) and "Baim" would not lead one to applicants' invention as described in the amended claims submitted herein.

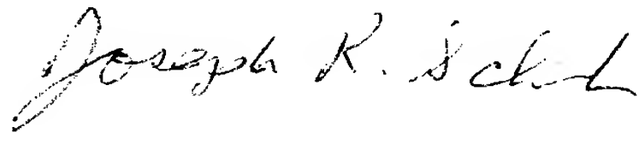
Further, these references provide no reasonable expectation of success, even if their teachings are combined as asserted by the Office.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness of the present claims over "Baim" in view of Delyani(A) and Delyani(B). Accordingly, the aforementioned §103 objection should not be maintained against pending Claims 28, 35 and 75 to 79.

* * *

Claims 28, 35 and 75-79, as amended herein, should now be in condition for allowance. Favorable consideration and early allowance of these claims is requested. Applicants respectfully request a three-month extension of time to and including August 8, 2007 for filing a response to the February 8, 2007 Office Action in this matter. The Commissioner is hereby authorized to charge the $1020.00 fee for the requested three-month extension of time under 37 C.F.R. 1.16 and 1.17, together with any fees that may be required during the entire pendency of this application, to Deposit Account No. 19-1025.

Respectfully submitted,



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